

RECEIVED
CENTRAL FAX CENTER
JUL 23 2008

IN THE CLAIMS

Please amend the claims of the present application under the provisions of 37 C.F.R. §1.121(c), as indicated below:

1. (Currently amended): A modified release dosage form comprising of a high solubility active ingredient prepared by using dual retard technique to control the release of the high solubility active ingredient, said dosage form comprising a) micro matrix particles containing active ingredient(s) and one or more hydrophobic release controlling agent wherein the ratio of active ingredient(s) and hydrophobic release agent is in the range of 100:2.5 to 100:30, and b) a coating of one or more hydrophobic release controlling agents on said micro matrix particles wherein the ratio of micro-matrix particles and hydrophobic release controlling agent is in the range of ~~10:2.5 to 100:30~~ 100:2.5 to 100:30.

2. (Original): A dosage form as claimed in claim 1, is in the form of tablet.

3. (Previously presented): A dosage form according to claim 1, wherein the hydrophobic release controlling agents are selected from the group consisting of ammonio methacrylate copolymers type A and B as described in USP, methacrylic acid copolymer type A, B and C as described in USP, polyacrylate dispersion 30% as described in Ph. Eur., polyvinyl acetate dispersion, ethylcellulose, cellulose acetate, cellulose propionate (lower, medium or higher molecular weight), cellulose acetate propionate, cellulose acetate butyrate, cellulose acetate phthalate, cellulose triacetate, poly(methyl methacrylate), poly(ethyl methacrylate), poly(butyl methacrylate), poly(isobutyl methacrylate), poly(hexyl methacrylate), poly(isodecyl methacrylate), poly(lauryl methacrylate), poly(phenyl methacrylate), poly(methyl acrylate), poly(isopropyl acrylate), poly(isobutyl acrylate),

Application No: 10/630,348
Examiner: MERCIER, MELISA S

poly (octadecyl acrylate), waxes selected from the group consisting of beeswax, carnauba wax, microcrystalline wax, and ozokerite; fatty alcohols selected from the group consisting of cetostearyl alcohol, stearyl alcohol; cetyl alcohol and myristyl alcohol; and fatty acid esters selected from the group consisting of glyceryl monostearate; glycerol monooleate, acetylated monoglycerides, tristearin, tripalmitin, cetyl esters wax, glyceryl palmitostearate, glyceryl behenate and hydrogenated castor oil.

4. (Previously presented): A dosage form according to claim 3, wherein said hydrophobic release controlling agents are selected from ammonio methacrylate co-polymers.

5. (Previously presented): A dosage form according to claim 4, wherein ammonio methacrylate co-polymers are selected from the group consisting of Ammonio Methacrylate Copolymer type B USP, Ammonio Methacrylate Copolymer type A USP and Polyacrylate dispersion 30% Ph. Eur.

6. (Canceled)

7. (Canceled)

8. (Canceled)

9. (Previously presented) A dosage form according to claim 1, wherein in micro matrix particles, the active ingredient and one or more hydrophobic release controlling agents are present in a ratio of from 100:2.5 to 100:20.

10. (Previously presented): A dosage form according to one of claims 1-5 wherein in micro matrix particles, the active ingredient can be less than or equal to 1500 mg.

Application No: 10/630,348
Examiner: MERCIER, MELISA S

11. (Previously presented): A dosage form according to claim 1, wherein a coating of one or more hydrophobic release controlling agents on said micro matrix particles are selected from the group comprising of ammonio methacrylate copolymers type A and B as described in USP, methacrylic acid copolymer type A, B and C as described in USP, polyacrylate dispersion 30% Ph. Eur., polyvinyl acetate dispersion, ethylcellulose, cellulose acetate, cellulose propionate (lower, medium or higher molecular weight), cellulose acetate propionate, cellulose acetate butyrate, cellulose acetate phthalate, cellulose triacetate, poly(methyl methacrylate), poly(ethyl methacrylate), poly(butyl methacrylate), poly(isobutyl methacrylate), poly(hexyl methacrylate), poly(isodecyl methacrylate), poly(lauryl methacrylate), poly(phenyl methacrylate), poly(methyl acrylate), poly(isopropyl acrylate), poly(isobutyl acrylate), poly(octadecyl acrylate), waxes selected from the group consisting of beeswax, carnauba wax, microcrystalline wax, and ozokerite; fatty alcohols -selected from the group consisting of cetostearyl alcohol, stearyl alcohol; cetyl alcohol and myristyl alcohol; and fatty acid esters selected from the group consisting of glyceryl monostearate; glycerol monooleate, acetylated monoglycerides, tristearin, tripalmitin, cetyl esters wax, glyceryl palmitostearate, glyceryl behenate and hydrogenated castor oil.

12. (Previously presented): A dosage form according to claim 11, wherein the hydrophobic release controlling agents are selected from fatty acid esters.

13. (Previously presented): A dosage form according to claim 12, wherein the fatty ester is selected from the group consisting of hydrogenated castor oil and glycerol distearate.

14. (Canceled)

Application No: 10/630,348
Examiner: MERCIER, MELISA S

15. (Canceled)

16. (Previously presented) A dosage form according to claim 1, wherein micro matrix particles and coating of one or more hydrophobic release controlling agents are present in a ratio of from 100:2.5 to 100:20.

17. (Previously presented): A dosage form according to claim 1, wherein the high solubility active ingredient is selected from the group consisting of antidiabetic agents, anti-histamines, anti-depressants, anti-viral agents, anesthetics, antacids, anti-arthritics, antibiotics, anti-psychotics, anti-spasmodics, anxiolytic agents, appetite suppressants, cardiovascular agents, cough suppressants, emollients, gastro-intestinal agents, growth regulators, respiratory stimulants, vitamins, angiotensin converting enzyme inhibitors, anti-asthmatics, anti-cholesterolemics, anti-convulsants, anti-depressants, anti-diarrhea preparations, anti-infective, anti-inflammatory agents, anti-nauseants, anti-stroke agents, anti-tumor drugs, anti-tussives, anti-uricemic drugs, amino-acid preparations, antiemetics, antiobesity drugs, antiparasitics, antipyretics, appetite stimulants, cerebral dilators, chelating agents, cholecystokinin antagonists, cognition activators, deodorants, dermatological agents, diuretics, erythropoietic drugs, fertility agents, synthetic hormones, laxatives, mineral supplements, neuroleptics, neuromuscular agents, peripheral vasodilators, prostaglandins, vaginal preparations, vaso-constrictors, vertigo agents, biguanides, sulphonylurease, meglitinides, PPAR gamma agonist [insulin sensitizers (thiazolidinedione)] and alpha-glucosidase inhibitors.

18. (Original): A dosage form according to claim 1, wherein the high solubility active ingredient is selected from the group comprising of metformin hydrochloride, phenformin, buformin, captopril, ranitidine hydrochloride, potassium chloride, clindamycin,

Application No: 10/630,348
Examiner: MERCIER, MELISA S

hydroxyurea, erythromycin lactobionate, vancomycin hydrochloride, balsalazide disodium, aminocaproic acid, lisinopril, tramadol, acetaminophen, ciprofloxacin, esters of ampicillin, sodium valproate, niacin, diltiazem, venlafaxine, isosorbide 5-imononitrate, isosorbide dinitrate, pentoxifylline, propranolol and quetiapine or pharmaceutically acceptable salts thereof.

19. (Original): A dosage form according to claim 1, wherein the dissolution of high solubility active ingredient is not more than 50% in 1 hour and from 25 to 90% is released in six hours.

20. (Original): A dosage form according to claim 1, wherein it reduces the chances of dose dumping, unnecessary burst effects and failure of the system.

21. (Previously presented): A dosage form according to claim 1, wherein the high solubility active ingredient is potent.

22. (Original): A dosage form according to claim 21, wherein it reduces the chances of dose dumping, unnecessary burst effects and failure of the system.

23. (Previously presented): A dosage form according to claim 21, where the high solubility potent active ingredient is selected from the group consisting of antidiabetic agents, antihistamines, anti-depressants, anti-viral agents, anesthetics, antacids, anti-arthritics, antibiotics, anti-psychotics, anti-spasmodics, anxiolytic agents, appetite suppressants, cardiovascular agents, cough suppressants, emollients, gastro-intestinal agents, growth regulators, respiratory stimulants, vitamins, angiotensin converting enzyme inhibitors, anti-asthmatics, anti-cholesterolemics, anti-convulsants, anti-depressants, anti-diarrhea preparations, anti-infective, anti-inflammatory agents, anti-nauseants, anti-stroke

Application No: 10/630,348
Examiner: MERCIER, MELISA S

agents, anti-tumor drugs, anti-tussives, anti-uricemic drugs, amino-acid preparations, antiemetics, antiobesity drugs, antiparasitics, antipyretics, appetite stimulants, cerebral dilators, chelating agents, cholecystokinin antagonists, cognition activators, deodorants, dermatological agents, diuretics, erythropoietic drugs, fertility agents, synthetic hormones, laxatives, mineral supplements, neuroleptics, neuromuscular agents, peripheral vasodilators, prostaglandins, vaginal preparations, vasoconstrictors, vertigo agents, biguanides, sulphonylurease, meglitinides, PPAR gamma agonist [insulin sensitisers (thiazolidinedione)] and alpha-glucosidase inhibitors.

24. (Original): A dosage form according to claim 21, wherein the high solubility potent active ingredient is selected from the group comprising of benzotropine mesylate, distigmine bromide, flupenthixol dihydrochloride, formotexol fumarate, glycopyrrate, granisetron hydrochloride, bisoprolol fumarate, atropine sulphate, azatadine maleate, carteolol HCl, brompheniramine maleate, nicotine, oxybutamine chloride, perinodopril erbumine, pilocarpine, poldine methyl sulfate and zalcitane.

25. (Original): A dosage form according to claim 1, can be given twice a day or more preferably can be given once a day.

26. (Original): A dosage form according to claim 1, is used for human beings.

27. (Original): A dosage form according to claim 1, wherein the high solubility active ingredient is niacin.

28. (Previously presented): A modified release dosage form according to claim 27, wherein the composition of the micromatrix particles and coated micromatrix particles is as follows--Micro matrix particles--Niacin 75% w/w to 99% w/w EUDRAGIT RS®

Application No: 10/630,348
Examiner: MERCIER, MELISA S

(Ammonio Methacrylate Copolymer type B USP) 1% w/w to 25% w/w Coated micro matrix particles Micro matrix particles 70% w/w to 99% w/w Hydrogenated castor oil 1% w/w to 30% w/w Magnesium stearate 0% w/w to 2% w/w.

29. (Original): A dosage form according to claim 1, wherein the high solubility active ingredient is sodium valproate.

30. (Previously presented): A process for the preparation of a modified release dosage form comprising a) preparing a micro matrix particles containing high solubility active ingredient and one or more hydrophobic release controlling agent wherein the ratio of active ingredient(s) and hydrophobic release controlling agent is in the range of 100:2.5 to 100:30 and b) coating the said micromatrix particles containing high solubility active ingredient and one or more hydrophobic release controlling agent, wherein the ratio of micro-matrix particles and hydrophobic release controlling agent is in the range of 100:2.5 to 100:30.

31. (Previously presented): A modified release dosage form comprising of a metformin hydrochloride prepared by using dual retard technique to control the release of metformin, said dosage form comprising a) micro matrix particles containing metformin hydrochloride and one or more hydrophobic release controlling agent wherein the ratio of active ingredient(s) and hydrophobic release controlling agent is in the range of 100:2.5 to 100:30 and b) coating of one or more hydrophobic release controlling agent on micro matrix particles, wherein the ratio of micro-matrix particles and hydrophobic release controlling agent is in the range of 100:2.5 to 100:30.

32. (Original): A dosage form as claimed in claim 31, is in the form of tablet.

Application No: 10/630,348
Examiner: MERCIER, MELISA S

33. (Previously presented): A dosage form according to claim 31, wherein the hydrophobic release controlling agents employed for the micro matrix particles are selected from the group consisting of ammonio methacrylate copolymers type A and B as described in USP, methacrylic acid copolymer type A, B and C USP, polyacrylate dispersion 30% Ph. Eur., polyvinyl acetate dispersion, ethylcellulose, cellulose acetate, cellulose propionate (lower, medium or higher molecular weight), cellulose acetate propionate, cellulose acetate butyrate, cellulose acetate phthalate, cellulose triacetate, poly(methyl methacrylate), poly(ethyl methacrylate), poly(butyl methacrylate), poly(isobutyl methacrylate), poly(hexyl methacrylate), poly(isodecyl methacrylate), poly(lauryl methacrylate), poly(phenyl methacrylate), poly(methyl acrylate), poly(isopropyl acrylate), poly(isobutyl acrylate), poly(octadecyl acrylate), waxes selected from the group consisting of beeswax, carnauba wax, microcrystalline wax, and ozokerite; fatty alcohols selected from the group consisting of cetostearyl alcohol, stearyl alcohol; cetyl alcohol and myristyl alcohol; and fatty acid esters selected from the group consisting of glyceryl monostearate; glycerol monooleate, acetylated monoglycerides, tristearin, tripalmitin, cetyl esters wax, glyceryl palmitostearate, glyceryl behenate and hydrogenated castor oil.

34. (Previously presented): A dosage form according to claim 33, wherein the hydrophobic release controlling agents are selected from ammonio methacrylate copolymers.

35. (Previously presented): A dosage form according to claim 34, wherein the ammonio methacrylate co-polymers are selected from the groups consisting of Ammonio Methacrylate Copolymer type B USP, Ammonio Methacrylate Copolymer type A USP and Polyacrylate dispersion 30% Ph. Eur.

36. (Canceled)

JUL 23 2008

Application No: 10/630,348
Examiner: MERCIER, MELISA S

37. (Canceled)

38. (Canceled)

39. (Previously presented) A dosage form according to claim 31, wherein in micro matrix particles, metformin hydrochloride and one or more hydrophobic release controlling agents are present in a ratio of from 100:2.5 to 100:20.

40. (Previously presented): A dosage form according to one of claims 31-34, wherein in micro matrix particles, metformin hydrochloride can be less than or equal to 1500 mg.

41. (Previously presented): A dosage form according to claim 31, wherein the coating of one or more hydrophobic release controlling agents on said micro matrix particles are selected from the group consisting ammonio methacrylate copolymers type A and B as described in USP, methacrylic acid copolymer type A, B and C USP, polyacrylate dispersion 30% Ph. Eur., polyvinyl acetate dispersion, ethylcellulose, cellulose acetate, cellulose propionate (lower, medium or higher molecular weight), cellulose acetate propionate, cellulose acetate butyrate, cellulose acetate phthalate, cellulose triacetate, poly(methyl methacrylate), poly(ethyl methacrylate), poly(butyl methacrylate), poly(isobutyl methacrylate), poly(hexyl methacrylate), poly(isodecyl methacrylate), poly(lauryl methacrylate), poly(phenyl methacrylate), poly(methyl acrylate), poly(isopropyl acrylate), poly(isobutyl acrylate), poly(octadecyl acrylate), waxes selected from the group consisting of beeswax, carnauba wax, microcrystalline wax, and ozokerite; fatty alcohols selected from the group consisting of cetostearyl alcohol, stearyl alcohol; cetyl alcohol and myristyl alcohol; and fatty acid esters selected from the group consisting of glyceryl

Application No: 10/630,348
Examiner: MERCIER, MELISA S

monostearate; glycerol monooleate, acetylated monoglycerides, tristearin, tripalmitin, cetyl esters wax, glyceryl palmitostearate, glyceryl behenate and hydrogenated castor oil.

42. (Previously presented): A dosage form according to claim 40, wherein the hydrophobic release controlling agents are selected from fatty acid esters.

43. (Previously presented): A dosage form according to claim 42, wherein fatty acid ester is selected from the group consisting of hydrogenated castor oil and glycerol distearate.

44. (Canceled)

45. (Canceled)

46. (Previously presented): A dosage form according to claim 31, wherein micro matrix particles and coating of one or more hydrophobic release controlling agents are present in a ratio of from 100:2.5 to 100:20.

47. (Previously presented): A modified release dosage form according to claim 31, wherein the composition of the micromatrix particles and coated micromatrix particles is as follows--Micro matrix particles--Metformin hydrochloride 75% w/w to 99% w/w Ammonio Methacrylate Co-polymer type B USP 1% w/w to 25% w/w Coated micro matrix particles Micro matrix particles 70% w/w to 99% w/w Hydrogenated castor oil 1% w/w to 30% w/w Magnesium stearate 0% w/w to 2% w/w.

48. (Original): A dosage form according to claim 31, wherein the dissolution of metformin hydrochloride is not more than 50% in 1 hour, from 30 to 90% in four hours and not less

Application No: 10/630,348
Examiner: MERCIER, MELISA S

than 65% in twelve hours.

49. (Original): A dosage form according to claim 31, is once a day oral formulation.

50. (Original): A dosage form according to claim 31, is used for human beings.

51. (Original): A dosage form according to claim 31, wherein the maximum plasma metformin concentration is achieved between 700 ng/ml and 2500 ng/ml.

52. (Previously presented): A dosage form according to claim 51, wherein the maximum plasma metformin concentration is achieved between 900 ng/ml and 2400 ng/ml.

53. (Previously presented): A dosage form according to claim 51, wherein the maximum plasma metformin concentration is achieved between 1000 ng/ml and 2350 ng/ml.

54. (Original): A dosage form according to claim 31, wherein the modified release metformin formulation for once daily administration exhibit in vivo mean dissolution time (MDT) of approximately 4 hours to 6 hours.

55. (Original): A dosage form according to claim 31, wherein the minimum plasma metformin concentration (at 24 hours) ranges between 0 and 450 ng/ml after oral administration.

56. (Original): A dosage form as claimed in claim 1, wherein the said dosage form is used to increase the payload of high solubility active ingredient.

57. (Original): A dosage form as claimed in claim 31, wherein the said dosage form is used

Application No: 10/630,348
Examiner: MERCIER, MELISA S

to increase the payload of metformin hydrochloride.

58. (Original): A dosage form as claimed in claim 1, wherein the said dosage form may optionally contain more than one high solubility active ingredient.

59. (Original): A dosage form as claimed in claim 31, wherein the said dosage form may optionally contain more than one antidiabetic active ingredient.

60. (Previously presented): A process for the preparation of a modified release dosage form comprising a) preparing a micro matrix particles containing metformin hydrochloride and one or more hydrophobic release controlling agent(s) wherein the ratio of metformin hydrochloride and hydrophobic release controlling agent is in the range of 100:2.5 to 100:30 and b) coating the said micro matrix particles containing metformin hydrochloride and one or more hydrophobic release controlling agent, wherein the ratio of micro-matrix particles and hydrophobic release controlling agent is in the range of 100:2.5 to 100:30.